NTP
National Toxicology Program

Research Concept: Naturally Occurring Asbestos and Related Mineral Fibers

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NTP Board of Scientific Counselors Meeting

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Nomination: Asbestos, naturally occurring and atypical forms

- Nominated by the National Center for Environmental Health/Agency for Toxic Substances and Disease Registry and the U.S. EPA based on:
  - Widespread community exposure in certain geographical areas
  - Insufficient toxicity data to characterize risk for non-commercial asbestiform mineral fibers
  - Need to better understand influence of mineralogy and morphology on mineral fiber toxicity
    - Particularly for non-asbestiform particles of similar chemical composition and dimension
- Requested studies of the Libby amphibole and materials representative of mineral fibers and particles at sites of recent public health concern

Background: Identification and Definitions

Asbestos: A generic commercial term for several silicate minerals occurring in the asbestiform habit

Asbestiform: A specific type of fibrous mineral habit in which the growth is primarily in one dimension and the crystals form naturally as long, flexible fibers…in separable bundles…*not all minerals having asbestiform habit are asbestos minerals*

Regulated asbestos minerals:

Asbestiform Variety	Non-asbestiform variety
Serpentine group	
chrysotile	antigorite
Amphibole group	
crocidolite	riebeckite
grunerite asbestos (amosite)	grunerite
anthophyllite asbestos	anthophyllite
tremolite asbestos	tremolite
actinolite asbestos	actinolite

"Naturally Occurring Asbestos"

- Regulated asbestos minerals, plus
  - Fibrous forms of the amphiboles winchite, richterite, edenite, others?
- Mixture of elongated particles of varying size, shape, chemical composition
  - Asbestiform fibers, acicular and prismatic crystals, cleavage fragments
  - Associated with other non-fibrous minerals (e.g. calcite, quartz)
- Chemical composition can vary along length of a given particle
- Associated with specific geologic formations
- Relatively widespread but not fully described or mapped

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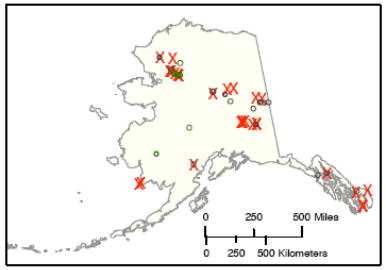
ATSDR
AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY

Naturally Occurring Asbestos Locations in the Contiguous USA and Alaska and the 100 Fastest Growing U.S. Counties

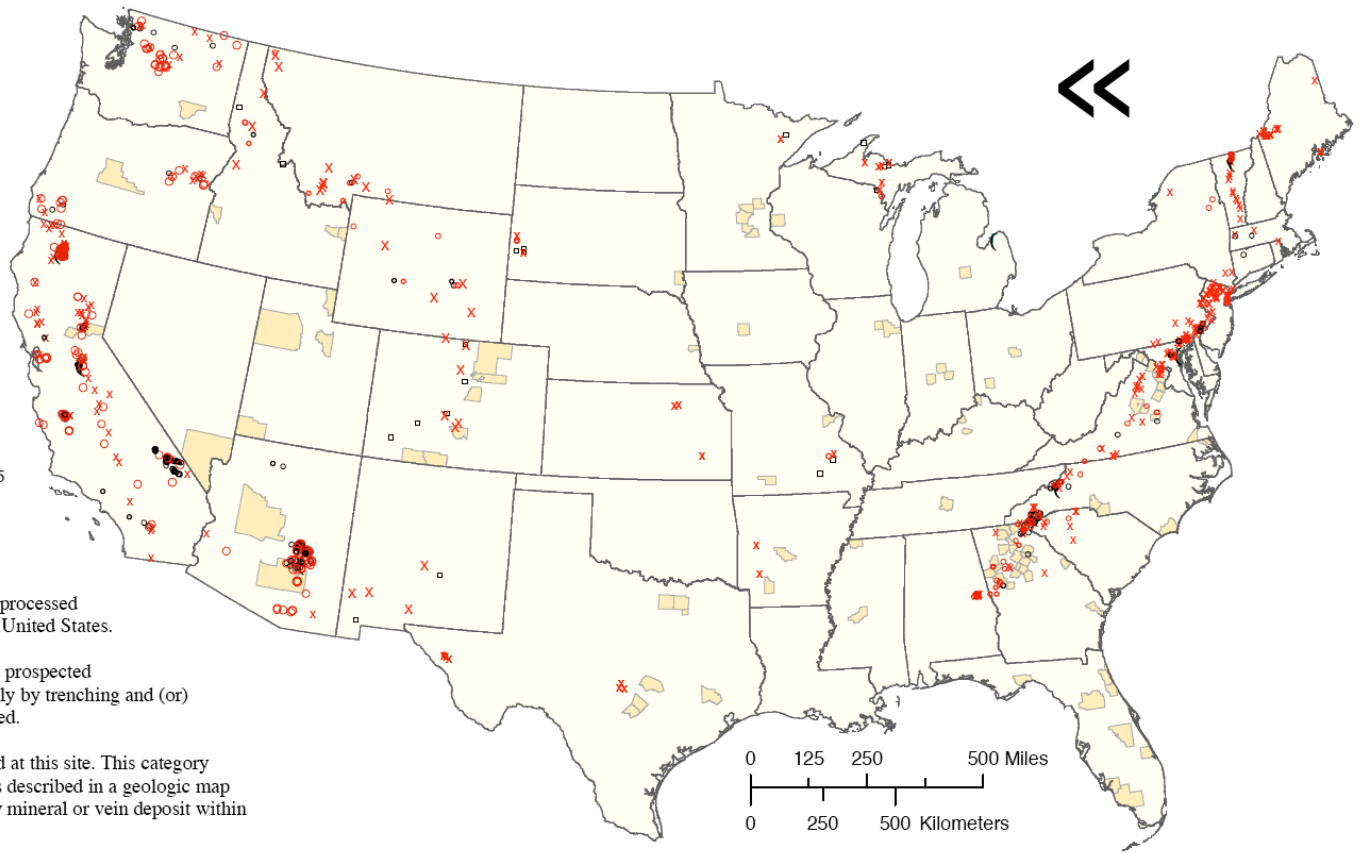
GRASP
GEOSPATIAL RESEARCH, ANALYSIS & SERVICES PROGRAM



Asbestos does not occur naturally in Hawaii.

- Prospect[1,2,3,4]
- Past producer[1,2,3,4]
- Former Processing Plant[4]
- Occurrences of Asbestos[1,2,3,4]
- Fibrous Amphiboles[2,3]
- Top 100 fastest growing county[5]

Projection: Lambert Conformal Conic, NAD 83
(preserves local directions)



Former Processing Plants are plants that once processed asbestos. Asbestos is no longer processed in the United States.

Prospect indicates that the asbestos deposit was prospected (evaluated) for possible commercial use, typically by trenching and (or) drilling, but the deposit was not further developed.

Occurrence indicates that asbestos was reported at this site. This category includes (1) sites where asbestos-bearing rock is described in a geologic map or report; and (2) asbestos noted as an accessory mineral or vein deposit within another type of mineral deposit.

Past Producer is an asbestos mine that once operated in the U.S. but is currently closed; the equipment or structures may have been removed or abandoned. There are no current producers in the United States.

Fibrous amphibole indicates sites where minerals of the amphibole mineral group have been described as fibrous in the geologic literation. The reports on these locations do not mention asbestos but these sites indicate geologic settings with the potential to host asbestos.

[1]U.S.Geological Survey. 2005 Ver. 2, Reported historic asbestos mines, historic asbestos prospects, and natural asbestos occurrences in the eastern United States. Reston, Virginia. [cited 2006 March]. Available at http://pubs.usgs.gov/of/2005/1189/.

[2]U.S.Geological Survey. 2006, Reported historic asbestos prospects, and natural asbestos occurrences in the central United States. Reston, Virginia. [cited 2006 August]. Available at http://pubs.usgs.gov/of/2006/1211/.

[3]U.S.Geological Survey. 2007, Reported historic asbestos mines, historic asbestos prospects, and natural asbestos occurrences in the Rocky Mountain States of the United States (Colorado, Idaho, Montana, New Mexico, and Wyoming. Reston, Virginia. [to be published].

[4]U.S. Geological Survey. 2005. Mineral resources data system. Reston, Virginia. [cited 2005 July 6]. Available at http://tin.er.usgs.gov/mrds/.

[5]U.S. Bureau of the Census, Population Division. 2004. Housing unit estimates for the 100 fastest growing U.S. counties between July 1, 2002 and July 1, 2003: percent change between July 1, 2002 to July 1, 2003. Washington, D.C: U.S. Department of Commerce. July 23, 2004 [cited 2005 Jul 5]. Available at: http://www.census.gov/popest/housing/tables/HU-EST2003-06.xls.

Kaplan and Neurath - 5/2007

<project=01972><userid=bck2><geo=USA><keywords=asbestos, natural, population>

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Background: Health Effects of Asbestos

- Known human carcinogen
  - Lung cancer, pleural and peritoneal mesothelioma, laryngeal cancer
  - Suggestive but inadequate evidence for other sites (e.g. GI, colorectal)
  - Risk estimates based on lung cancer and mesothelioma from epidemiologic studies
  - Supporting animal studies
- Hallmark non-malignant pulmonary disease
  - Asbestosis, pleural abnormalities
- Emerging evidence for cardiovascular and autoimmune disease
- Mechanisms of toxicity
  - Physical damage to cells, nuclear machinery
  - ROS generation leading to oxidative stress, DNA damage, aberrant signaling pathways
  - Importance of chemical composition, size, shape, durability, clearance
- Amphibole asbestos more potent than chrysotile

Some Exposure Situations of Current Concern

- Libby, MT and Libby “Sisters” sites
  - W.R. Grace Zonolite mine, early 1920s-1990, shipped >5M tons vermiculite ore to >200 processing facilities in 39 U.S. states
  - Vermiculite ore associated with asbestiform amphiboles, primarily winchite, richterite, tremolite, and non-asbestiform varieties of these and other minerals
  - Significant excess mortality from malignant and non-malignant respiratory disease in former mine workers and residents
- El Dorado Hills, CA
  - Actinolite, tremolite found in air/soil at schools, residential and recreation areas
- Minnesota iron range
  - Fibrous amphiboles linked to mesothelioma in taconite mine workers
- Construction and outdoor work/recreation in areas of NOA formations
- Commercial products
  - Vermiculite attic insulation, aggregates (gravel,fill)

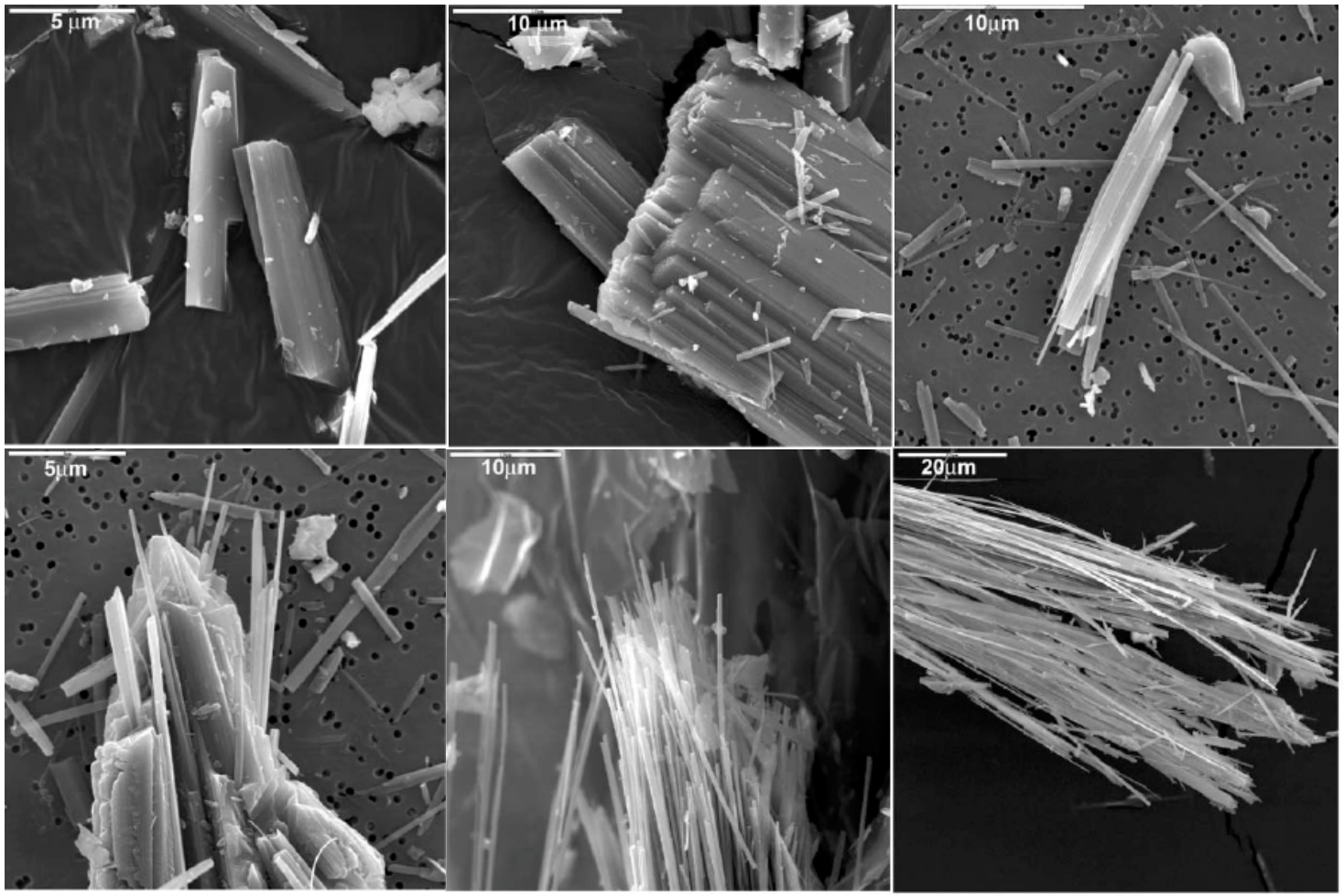
Rationale for Proposed Research Program

- Significance and public health impact
  - Continuing exposure in certain occupations and geographical areas
  - Knowledge gaps regarding fiber characteristics and relationship to toxicity
  - Public concern, particularly for low dose and episodic exposures, and for children's exposures
  - Identified research need by EPA, NCEH/ATSDR, NIOSH, CPSC
  - Provide supporting data for ongoing risk assessment and public health investigations
    - Libby-specific, EPA IRIS, NOA sites
- Address lingering uncertainties in risk assessment
  - Hazard characterization for "non-regulated" mineral fibers
  - Dose-response assessment for well characterized mineral fibers
  - Relative potency of diverse mineral structures

Key Issues to Address

- Particle dimension and morphology
  - Thorough characterization at all phases of study
- Durability
  - Relative biopersistence of different elongated particles
- Dosimetry
  - Optimal dose metric(s) for evaluating risk
  - Extrapulmonary tissue burden
- Relative potency of non-asbestiform particles meeting regulatory fiber definition
  - Can only be directly addressed with relatively pure samples with same mineral composition and particle dimension
  - Indirectly addressed with multiple samples with range of dimensions and composition

Electron micrographs of typical morphological types of Vermiculite Mountain amphiboles. The morphologies range from prismatic crystals (upper left) to long fibers and bundles (lower right).



From Meeker *et al*. (2003), American Mineralogist 88, 1955.

Hypotheses to Evaluate

- Cumulative dose, as measured by lung fiber burden, is the most appropriate dose metric for predicting carcinogenic and non-carcinogenic effects of mineral fibers
- The cumulative dose-response and potency differs among representative natural mineral fibers
- Particles with similar dimensions and of similar chemical composition have equivalent toxic and carcinogenic potencies.
  - Durability (in vitro) and biopersistence (in vivo) of natural mineral fibers, a function of both mineralogy and morphology, is the primary determinant of toxic and carcinogenic potency
  - Chemical composition (mineralogy) is of secondary importance in determining toxic and carcinogenic potency

Proposed Research Program

- Identification and selection of natural mineral fibers
  - Libby amphibole composite sample
  - Commercial source of amosite asbestos
  - Select 2-3 other site-specific natural mineral fiber samples from among:
    - Tremolite, actinolite, winchite, erionite
- Physical and chemical characterization of test materials
  - Particle mineralogy and morphology
- Assessment of fiber durability
  - *In vitro* dissolution and *in vivo* biopersistence studies
- Subchronic and chronic inhalation toxicology studies
  - Multiple dose with designs that test cumulative dose concept

Some Study Design Issues

- Minimal processing of test materials
  - Potential loss of bioactive structures, cations, altered surface chemistry
- Selection of chronic study doses
  - Based on short-term biopersistence studies?
- Duration of exposure
  - Address susceptibility due to early life exposure
- Chronic study exposure regimens
  - Include groups with variable concentration (C) and exposure durations (T) but with equivalent C x T

Questions and Comments